Niger J Paed 2013; 40 (1): 75 - 78

ORIGINAL

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Erythrocyte indices of iron status in children with cyanotic congenital heart disease at the University College Hospital, Ibadan.

DOI:http://dx.doi.org/10.4314/njp.v40i1.14
Accepted: 30th July 2012

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Abstract *Background* Iron (Fe) deficiency is a known feature of cyanotic congenital heart disease (CCHD) and may worsen symptoms. The prevalence of iron deficiency among children with CCHD at the University College Hospital (UCH), Ibadan is unknown. Erythrocyte indices of iron status are easier and less expensive to determine than serum iron, serum ferritin and total iron binding capacity, which are the standard tests of iron deficiency.
Objectives: To examine the erythrocyte indices of iron status in children with CCHD in UCH, and determine the prevalence of iron deficiency among such patients, by comparing the values obtained with established reference values.
Subjects and Methods: The packed cell volume (PCV), haemoglobin (Hb), mean corpuscular volume (MCV), mean corpuscular haemoglobin concentration (MCHC) and red cell distribution width (RDW) of 40 children with CCHD, determined using a Sysmex 1000X1 Coulter counter, were compared with standard reference values.
Results: Mean±SD values obtained were – PCV: 58.6±11.6%. MCV: 80.7±12.1 µm^3, MCH: 25.9±9.5g/dl, MCHC: 30.9±4.1 and RDW: 20.5.5±12.6%.
Lower-than-normal values for MCV, MCH and MCHC were found in 33.5%, 42.5% and 72.5% of patients, respectively, while 77.5% had higher-than-normal values for RDW. However, using the criteria based on a combination of RDW and MCV, 35% of patients were iron deficient.
Conclusion: A large proportion of Nigerian children with CCHD appear to be iron deficient and are therefore likely to benefit from routine iron therapy.

Key words: Cyanotic Congenital Heart Disease; Erythrocyte indices; Iron deficiency.

Introduction

Fallot's tetralogy is the commonest cyanotic congenital heart disease (CCHD) worldwide. It is characterised by cyanosis of variable severity, associated with symptoms such as decreased effort tolerance, squatting, hypercyanotic spells, and in severely polycythaemic patients, bleeding diatheses and cerebrovascular events. Iron (Fe) deficiency is known to be a feature of CCHD[1, 2] and may worsen symptoms. Iron therapy is therefore recommended for those who demonstrate this feature. The iron status of children with CCHD seen at the University College Hospital (UCH), Ibadan, has never been studied. Iron therapy is not routinely administered to such children at the UCH. Many are extremely polycythaemic, by virtue of either the severity, or the chronicity of their hypoxia, together with the fact that the time interval between diagnosis and surgery, whether palliative or definitive, is often prolonged for logistic or technical reasons. Iron therapy might benefit some of these patients, particularly those in whom delays between diagnosis and surgery may be inevitable because of other contingencies. A study of the iron status of children with CCHD was therefore thought to be germane, in that results of the study would stimulate the formulation of guidelines as to the need or otherwise for iron therapy in patients with CCHD in general, and Fallot's tetralogy in particular.

Although determination of serum iron, serum ferritin and total iron binding capacity are the standard tests of iron deficiency, they are expensive and not routinely available. We therefore decided to use erythrocyte indicators of iron status as a starting point.

Objectives

The study aimed to:

1. Examine the erythrocyte indices of iron status in children with CCHD in UCH,
2. Determine the prevalence of iron deficiency among such patients, by comparing the values obtained in one with established reference values.

Materials and methods

Forty patients of the Paediatric Cardiology Unit of the UCH, Ibadan with a diagnosis of CCHD whose haematological data were complete were recruited into the study. Each patient had undergone a thorough clinical evaluation with special reference to the cardiovascular system (CVS), along with chest radiography, electrocardiography and 2-dimensional (2-D) echocardiography, in order to establish the specific diagnosis. Their packed cell volume (PCV), haemoglobin (Hb), mean corpuscular volume (MCV), mean corpuscular haemoglobin concentration (MCHC) and red cell distribution width (RDW) were determined using a a Sysmex 1000XI Coulter counter. Each patient's Hb genotype was also determined. Normal reference ranges for each parameter were obtained from table 1, (adapted from Pesce.[3]) Patients were adjudged to be iron deficient according to criteria combining the use of `MCV and RDW, ie if both the MCV was lower than normal, and RDW was higher than normal for the age[4].

Table 1: Reference ranges for haematological tests.[3]

Age	1-14days	>14days	>28days – 5years	>5years
Haematocrit (%)	48–65	28–42	35–45	35–45
Haemoglogbin (g)	14.5–22.5	9.0–14.0	11.5–15.5	11.5–15.5
Mean corpuscular volume (μ m^3)	95–121	70–86	70–86	77–95
Mean corpuscular haemoglobin (pg/cell)	28–40	28–40	24–30	25–33
Mean corpuscular haemoglobin concentration (g/dl)	28–38	29–37	30–36	31–37
Red cell distribution width (%)	11 - 14.0	11- 14.0	11 - 14.0	11 - 14.0

Data Handling

The data were entered into an Excel spread-sheet. and analysed using SPSS 17.0 for Windows (SPSS Inc., Chicago, USA, 2010). Ranges, means and standard deviations were computed and compared with standard reference values using the Students t test. The level of significance was taken as $p<0.05$.

Results

There were 23 males and 17 females and their ages ranged from 1 to 162 (median = 48) months. Table 2 shows that the mean ages and weights of the males did not differ significantly from those of the females.

Table 2: Mean age and weight of study patients

	Male (23) Mean	SD	Female (17) Mean	SD	p
Mean Age (months)	67.5	46.4	54.3	43.9	0.402
Mean weight (kg)	15.6	4.3	11.9	9.0	0.218S

Fallot's tetralogy formed the majority - 36 (90 %) of the patients, followed by Tricuspid atresia (TA) - 3 (7.5%).and Transposition of the Great Arteries (TGA) - 1 (2.5%).

The patients' haematological profiles are depicted in Table 3

Table 3: Haematological profile of study patients

	Mean	SD	Median	Minimum	Maximum
Haematocrit (%)	58.6	11.6	59.0	29.0	85.0
Haemoglobin (g)	17.0	4.0	16.9	7.2	22.9
Mean corpuscular volume (μ m^3)	80.7	12.1	80.0	59.0	101.0
Mean corpuscular haemoglobin (pg/cell)	25.9	9.5	23.8	16.7	74.3
Mean corpuscular haemoglobin concentration (g/dl)	30.9	4.1	29.9	26.4	45.6

Table 4 shows that the frequencies of patients with values suggestive of Fe deficiency in each parameter were: MCV 37.5%, MCH 42.5%, MCHC 72.5%, and RDW 77.5%.

Table 4: Distribution of patients' haematological parameters

	Patients' values Low N	%	Normal N	%	High N	%
Haematocrit (%)	2	5.8	6	15.0	32	80.0
Haemoglogbin (g)	7	17.5	7	17.5	26	65.0
Mean corpuscular volume (μ m^3)	15	**37.5**	24	60.0	1	2.5
Mean corpuscular haemoglobin (pg/cell)	17	**42.5**	20	50.0	3	7.5
Mean corpuscular haemoglobin concentration (g/dl)	29	**72.5**	11	27.5	0	0.0
Red cell distribution width (%)	0	0.0	9	22.5	31	**77.5**

Figures in bold type represent the percentages of patients with values suggestive of iron deficiency

However Table 5 shows that using the classification based on RDW and MCV by Bessman *et al*,[4] which is the criterion adopted for this study, only 35% of the patients met the criteria for iron deficiency.

Table 5: Distribution of patients by MCV and RDW (indices of iron deficiency)

Mean corpuscular volume (μm^3)	Red cell distribution width (%) Normal N	% of all patients	High N	% of all patients	Total N	% of all patients
Low	1	2.5	14	35.0	15	37.5
Normal	7	17.5	17	42.5	24	60.0
High	1	2.5	0	0.0	1	2.5
Total	9	22.5	31	77.5	40	100.0

Using the classification based on RDW and MCV[4]from the above table 35.0% of the patients met the criteria for iron deficiency.

Table 6 shows that 40.6% of patients who had a high PCV were also iron deficient, using the criteria of Bessman *et al*[4], whereas none of patients with PCVs within the normal range, were iron deficient.

Table 6: Relationship between haematocrit level and presence of iron deficiency

Haematocrit	Iron deficiency Absent		Iron deficiency Present		Total	
	N	%	N	%	N	%
Low	1	50.0	1	50.0	2	100.0
Normal	6	100.0	0	0.0	6	100.0
High	19	59.4	13	40.6	32	100.0
Total	26	65.0	14	35.0	40	100.0

Chi square = 0.271, p = 0.603

Discussion

The subjects of this study were majorly patients with Fallot's tetralogy, which is to be expected, being the most common CCHD. The apparent 'under-representation' of TGA and TA, though indeed known to be much less common than Fallot's tetralogy, may be because some whose data were not complete were excluded from analysis.

Children with CCHD often experience severe hypoxaemia which may cause damage to the organs, particularly; the lungs, kidneys, musculoskeletal system and the central nervous system (CNS). A major compensatory mechanism to combat tissue hypoxaemia is secondary erythropoiesis with consequent increase in the red cell mass.[5, 6] This study showed that 32 (80.0%) of the cases had high haematocrit values. Iron deficiency is reported to be common in individuals with CCHD even in the presence of high haematocrit levels.[2,7, 8] These groups of children are often assumed not to be iron deficient because of the elevated red cell mass.

The use of simple red cell indices has been shown to be effective in identifying iron deficiency in individuals suspected to be deficient in iron.[1] Measurement of haematocrit, haemoglobin concentration, MCV, MCHC and peripheral blood film examination are easy to perform, relatively inexpensive and are effective in identifying iron deficiency when present.[1, 9] These methods were employed in this study and in the absence of more expensive tests like serum transferrin and serum ferritin, 14 (35%) of the 40 children with CCHD with iron deficiency were identified.

The prevalence obtained in this study is similar to the 37% prevalence reported by Kaemmerer, *et al*[7] in 52 German adults with CCHD. The figure is however much higher than the 16.9% quoted in another report from Kenya among 112 children with CCHD.[2] The findings in this study are therefore consistent with previous reports showing that iron deficiency is a common feature in patients with CCHD. Notably, iron deficiency was present in 40.6% of children in the present study with high PCV levels but in none of the 6 patients whose PCVs were normal. This proportion is high enough for concern and might justify a practice of instituting judicious iron therapy in patients with high PCVs , on the assumption that deficiency is likely to be present.

CCHD is known to be associated with a reduction in oxygen delivery to the tissues. Iron deficiency in CCHD has been shown to be associated with a further reduction in oxygen delivery to the tissues.[10] This further worsens the tissue hypoxaemia in individuals with CCHD. Clear recommendations for the supplementation of iron in children with CCHD are lacking. Our findings suggest that iron deficiency is common in Nigerian children with CCHD. Further studies using the gold-standard tests would still be required in order to verify the figures obtained in this study. In the interim, it is recommended that all children with CCHD should have routine assessment of the simple haematological indices for prompt detection and judicious treatment of iron deficiency.

Conflict of Interest: None
Funding: None

Acknowledgement

I wish to acknowledge Dr AE Orimadegun for assistance in the preparation of the manuscript.

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